

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln . No. 10/550,366

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Conf. No. 7973

Applicants: Hu et al.

Title: AUTOMATED METHOD
FOR IDENTIFYING
LANDMARKS WITHIN AN
IMAGE OF THE BRAIN

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Art Unit: 2624

Examiner: Wenpeng CHEN

Attorney Docket: 8249-85693

Customer No.: 22242

Mail Stop AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE TO OFFICE ACTION

Sir:

This Amendment and Response to Office Action is submitted in response to the May 29, 2009 Office Action. A response to the May 29, 2009 Office Action expires on August 29, 2009. Accordingly this Amendment and Response to Office Action is being timely filed.

Amendments to the specification begin on page 2 of this paper.

Amendments to the drawings begin on page 4 of this paper and include replacement sheets.

Amendment to the claims begin on page 5 of this paper.

Remarks/Arguments begin on page 11 of this paper.

AMENDMENTS TO THE SPECIFICATION

Please replace paragraph beginning at page 1 line 7 with the following amended paragraph:

-- The Talairach transformation is widely used for analysis of neurological images. It involves identifying eight landmarks, which are used to define a coordinate system. The Talairach landmarks subdivide the brain into 12 cuboids, and the Talairach transformation is to warp the images within each cuboid linearly. In this way the brain images are normalised by a three-dimensional piece-wise linear warping. This scheme has several applications, in particular because it makes it possible to compare neurological images from different individuals. One improvement on this scheme, while following its conceptual rationale, is the improvement of the definitions of the landmarks, to give "modified Talairach landmarks" (as defined in the article "Modified Talairach Landmarks", W. L. Nowinski, Acta Neurochirurgica, 2001, 143, p1045 - 1057, ~~the disclosure of which is incorporated herein by reference~~). In summary, the modified Talairach landmarks are derived by introducing three intercommissural distances: central, internal and tangential. Although these modified Talairach landmarks are conceptually equivalent to the original Talairach landmarks, they have several advantages and overcome some limitations of the original Talairach landmarks. --

Please replace paragraph beginning at page 5 line 2) with the following amended paragraph:

-- From this data, the midsagittal plane (MSP) is determined. This is preferably done using the method disclosed in WO02/069827, "Method and apparatus for determining symmetry in 2D and 3D images", by Hu and Nowinski (~~the disclosure of which is incorporated herein by reference~~). In summary, the method disclosed in WO02/069827 includes the steps of (1) determining axial slices to be further processed for fissure line segments, (2) approximating fissure line segments in axial slices by

optimization of local symmetry index and fissure pattern measure, and (3) calculating the plane equation of MSP from the approximated fissure line segments via histogram analysis. However, the invention is not limited in this respect, and any other technique for determining the MSP may also be applied. Indeed, it would also be possible within the scope of the invention for the input data to specify the MSP. --

Please replace paragraph beginning at page 6 line 4 with the following amended paragraph:

-- The coordinates of the anterior commissure (AC) and posterior commissure (PC) are then determined automatically. This can be done by the method disclosed in WO02/43003, "Methods and apparatus for processing medical images", by Nowinski and Thirunavuukarasuu ~~(the disclosure of which is incorporated herein by reference)~~, although once more the invention is not limited in this respect. In summary, the method disclosed in WO02/43003 calculates the coordinates of the AC and PC using peaks and valleys of a graph of the density profile of the image measured along a line or peaks and valleys of a projection along a specified direction. --

Please replace paragraph beginning at page 7 line 16 with the following amended paragraph:

-- In step 3.2 an optimum threshold is determined, based on the range-constrained weighted variance thresholding method. This includes the following steps, which are explained in a separate patent application by two of the present inventors: "Methods and apparatus for binarizing images", Singapore patent application 200307531-4, by Q. M. Hu, Z. Hou, and W. L. Nowinski, which was still unpublished at the priority ~~data~~ date of the present application, ~~and the disclosure of which is incorporated by reference.~~ --

Serial No. 10/550,366

Attorney Docket No. 8249-85693

Response to Office Action dated August 27, 2009

In Reply to Office Action dated May 29, 2009

AMENDMENT TO THE DRAWINGS

Please replace the informal drawings Figs. 1-5 with the Replacement sheets 1/5 through 5/5 attached herewith as APPENDIX A:

AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Currently Amended) A computer-based method for locating one or more landmarks using an MR image of a brain, the method including the following automatic steps:

(a) identifying a region of interest (ROI) with a plane of the MR image, the plane containing the landmark(s);

(b) binarising the plane of the MR image into foreground and background voxels based on at least one threshold selected using anatomical knowledge, the threshold being selected by maximizing a function which is a sum of variances of voxel intensities below and above the threshold;

(c) identifying a set of object voxels from the foreground voxels, the set of object voxels being formed by a sub-step of excluding from the foreground voxels a plurality of voxels which were only classified as foreground voxels due to proximity of cortical and non-cortical structures;

(d) identifying and restoring object voxels ~~from the background voxels lost during the excluding sub-step of step (c) due to partial volume effect and/or morphological erosion/opening, the restored object voxels being: object voxels located far from the skull, and lost due to the morphological opening operation(s); object voxels located around the boundaries of the object, and lost due to the morphological opening operation(s); and object voxels lost due to the partial volume effect; and~~

(e) identifying the one or more landmarks using the object ~~voxel~~ voxels identified in the steps (c) and (d).

2. (Original) A method according to claim 1 in which the step of identifying the object voxels is performed in two stages:

(i) morphological processing which excludes foreground voxels which may not be object voxels, and

(ii) restoring voxels which have been incorrectly excluded in the morphological processing.

3. (Original) A method according to claim 2 in which the step of identifying the object voxels further includes applying anatomical knowledge to identify the object voxels.

4. (Original) A method according to claim 3 in which the anatomical knowledge is knowledge about the expected shapes of cortical and/or non-cortical structures.

5. (Previously Presented) A method according to claim 1, wherein the threshold is selected by the steps of:

(i) using prior knowledge about the image to derive an intensity range of voxels in said region of interest;

(ii) obtaining a frequency distribution of intensities within said intensity range of voxels within said region of interest; and

(iii) using the frequency distribution to derive an intensity threshold.

6. (Cancelled)

7. (Currently Amended) A method according to claim [[6]] 1 in which said function is a weighted sum defined based on two constants W_1 and W_2 .

8. (Previously Presented) A method according to claim 7, comprising labeling possible values of voxel intensity by an integer index i and their respective frequencies by $h(i)$, and writing the lower and upper intensities respectively as r_{low} and r_{high} , wherein the weighted sum is given by

$$\theta_{RCLWV}(W_1, W_2) = \max_{r_i} (\Pr(C_1)D(C_1)W_1 + \Pr(C_2)D(C_2)W_2),$$

where $\Pr(\cdot)$ denotes class probability ($\Pr(C_1) = \sum_{i=r_{low}}^{r_i} h(i)$ and $\Pr(C_2) = \sum_{i=r_{high}+1}^{r_{high}} h(i)$), and

$D(C_1)$ and $D(C_2)$ are given by:

$$D(C_1) = (\mu_0 - \mu_T)^2, \text{ and } D(C_2) = (\mu_1 - \mu_T)^2,$$

where $\mu_T = \sum_{i=r_{low}}^{r_{high}} i \times h(i)$, $\mu_0 = \sum_{i=r_{low}}^{r_i} i \times h(i)$, and $\mu_1 = \sum_{i=r_{high}+1}^{r_{high}} i \times h(i)$.

9. (Previously presented) A method according to claim 1, wherein the steps (a) to (e) are performed repeatedly, in each set of steps identifying at least one corresponding landmark.

10. (Previously Presented) A method according to claim 1, wherein steps (a) to (d) are performed to locate A, P, L and R landmarks, and wherein

in step (a) the region of interest being defined within the AP plane; and

in step (e) the most anterior and most posterior of the object voxels being taken respectively as the vertical coordinates of the A and P landmarks respectively, and the extreme horizontal components of the object voxels are taken as the horizontal coordinates of the L and R landmarks respectively.

11. (Previously Presented) A method according to claim 10 wherein step (c) comprises:

performing at least one morphological opening operation on the binarized image obtained in step (b); and

classifying one or more voxels of the image(s) obtained by the opening operation(s) as object voxels or otherwise according to at least one criterion based on distances in the image(s) obtained by the opening operation(s) and anatomical knowledge.

12. (Previously Presented) A method according to claim 11 in which, prior to classifying the voxels, a maximum distance $\max D_{Skull}$ is obtained from a distance transform of the ROI.

13. (Cancelled)

14. (Previously Presented) A method according to claim 1 wherein steps (a) to (d) are performed to obtain an S landmark, the method comprising:

in step (a), defining the region of interest within a virtual plane obtained from a VPC coronal slice; and

in step (e), identifying the position of the S landmark as the most superior point of the object voxels.

15. (Previously Presented) A method according to claim 14 wherein step (c) comprises:

performing at least one morphological opening operation on the binarized image obtained in step (b); and

classifying as object voxels one or more voxels of the image(s) obtained by the morphological opening operation(s) if they belong to eight voxels immediately adjacent

to an object voxel and if their intensity value in the MR image is higher than a value defined in relation to a second threshold.

16. (Previously Presented) A method according to claim 1, wherein the set of steps (a) to (d) is performed to identify an I landmark, comprising:

in step (a), defining the region of interest within a VAC plane;

in step (e), defining the I landmark as the most inferior point of the object voxels.

17. (Previously Presented) A method according to claim 16 in which the threshold is obtained during a preceding process of locating an S landmark.

18. (Previously Presented) A method according to claim 16 in which, in step (c),

(i) at least one morphological opening operation, and/or

(ii) at least one seeding operation,

are performed on the binarized image obtained in step (b).

19. (Original) A method according to claim 18 in which, in step (c), one or more voxels of the image(s) obtained by the morphological opening operation(s) which are not presently classified as object voxels are re-classified as object voxels if they are one of the eight immediate neighbours of an object voxel and if their intensity value in the MR image is higher than a value defined in relation to a second threshold.

20. (Previously Presented) A method according to claim 16, wherein the left and right halves of the brain are treated separately, and the object voxels used to obtain the location of the I landmark relate to a selected half of the brain, the selected half of the brain having been selected based on a predefined criterion.

21. (Currently Amended) A system for locating one or more landmarks using an MR image of a brain, the system including:

an interface to receive data encoding the MR image; and

a processor arranged to perform the following steps:

(a) identifying a region of interest with a plane of the MR image, the plane containing the landmark(s);

(b) binarising the plane of the MR image into foreground and background voxels based on at least one threshold selected using anatomical knowledge, the threshold being selected by maximizing a function which is a sum of variances of voxel intensities below and above the threshold;

(c) identifying a set of object voxels from the foreground voxels, the set of object voxels being formed by a sub-step of excluding from the foreground voxels a plurality of voxels which were only classified as foreground voxels due to proximity of cortical and non-cortical structures;

(d) identifying and restoring object voxels ~~from the background voxels lost during the excluding sub-step of step (c) due to partial volume effect and/or morphological erosion/opening,~~ the restored object voxels being: object voxels located far from the skull, and lost due to the morphological opening operation(s); object voxels located around the boundaries of the object, and lost due to the morphological opening operation(s); and object voxels lost due to the partial volume effect; and

(e) identifying the one or more landmarks using the object voxels identified in the steps (c) and (d).

REMARKS/ARGUMENTS

In the Office Action of May 29, 2009, the Examiner objected to the drawings and specification for different informalities. Examiner rejected claims 1-20 under 35 U.S.C. §101 and §112, second paragraph, and under 35 U.S.C. §102 as anticipated by Brummer et al. ("Automated Detection of Brain Contours in MRI Data Sets") and under 35 U.S.C. §103 as unpatentable over Brummer in view of Nowinski et al. ("A locus-driven mechanism..."). Claims 8 was found to be allowable if rewritten to overcome §112 rejection.

Claims 1 – 21 were pending in this application. In this response, claims 1 and 21 have been amended to overcome the 35 U.S.C §112 objection. Claims 1 and 21 have been further amended to clarify the subject matter of steps (c) and (d). Support of these amendments can be found in the description page 10 line 27 – page 11 line 26 (which describes the steps of restoring the lost object voxels) and in the description page 9 line 3 (which shows an equation for selecting the intensity threshold by maximizing a function which is a sum of variances of voxel intensities below and above the threshold). In addition, claims 6 and 13 have been cancelled, and claim 7 amended to change the dependency.

No new matter has been added in the new claim set. Thus, claims 1 – 5, 7 – 21 remain pending.

Objection to the Drawings

Figs. 1 – 5 were objected to because they include handwriting. In view of the amendments made to Figs. 1 – 5, Applicant respectfully submits that the rejection of the drawings is now moot and should be withdrawn.

Objection to the Specification

Paragraphs 0002, 0035, 0036 and 0045 of the specification were objected to because they incorporate subject matter into the application by reference to either a publication or a foreign application or patent. Amendments were made to these paragraphs to overcome these objections and Applicant respectfully submits that no new matter has been added. In view of the amendments to the specification, the rejection of the specification is now moot and should be withdrawn.

Rejection to the Claims

Applicant appreciates the time and consideration provided by the Examiner in reviewing this application and allowing claim 8, but traverses the rejection of the claims at least for the following reasons.

Rejection of Claims 1 – 5, 7 – 20 Under 35 U.S.C. §101

Claims 1 – 5, 7 – 20 were rejected under 35 U.S.C. §101 because the claimed invention is allegedly directed to non-statutory subject matter. Applicants respectfully disagree with the Examiner.

According to the principle established by the case Abele 684 F. 2d, when a claim specifies data which clearly represents physical and tangible objects, namely the structures of bones, organs, and other body tissues, the transformation of that raw data into a particular visual depiction of a physical object on a display is sufficient to render that claim patent-eligible. Accordingly, one of Abele's dependent claims was held to be drawn to patent-eligible subject matter as the claim specified that "said data is X-ray attenuation data produced in a two dimensional field by a computed tomography scanner". This principle was upheld in the case Bilski 545 F.3d 943 (page 26 paragraph 1).

Claim 1 defines an MR image of a brain which clearly represents physical and tangible objects, namely the structures of the brain. Therefore, according to the principle established by the case Abele, claim 1, together with its dependent claims 2 – 5, 7 – 20, is patent-eligible. Accordingly, the rejection of the claims under 35 U.S.C. §101 should be withdrawn.

Rejection of Claims 1 – 5, 7 – 21 Under 35 U.S.C. §112

Claims 1 – 5, 7 – 21 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In view of the amendments made to claims 1 and 21, Applicant respectfully submits that the rejection under 35 U.S.C. §112 is now moot and should be withdrawn.

Rejection of Claims 1 and 21 Under 35 U.S.C. § 102(b)

Claims 1 and 21 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Brummer ("Automatic Detection of Brain Contours in MRI Data Sets," Marijn E. Brummer, et al. IEEE TRANSACTIONS ON MEDICAL IMAGING. VOL 12 NO. 2 JUNE 1993, pages 153 – 166). In view of the amendments to claims 1 and 21, it is respectfully submitted that the rejection under 35 U.S.C. §102(b) is now moot and should be withdrawn.

Amended claims 1 and 21 disclose, *inter alia*:

- (i) binarising the plane of the MR image into foreground and background voxels based on at least one threshold selected using anatomical knowledge, the threshold being selected by *maximizing* a function which is a sum of *variances of voxel intensities below and above the threshold*.
- (ii) identifying and *restoring* object voxels lost during the excluding sub-step of step (c), the restored object voxels being: object voxels located far

from the skull, and lost due to the morphological opening operation(s); object voxels located around the boundaries of the object, and lost due to the morphological opening operation(s); and object voxels lost due to the partial volume effect

Applicants respectfully submit that Brummer does not disclose feature (i). Instead, Brummer discloses obtaining a threshold for separating image objects from the background by *minimizing* a function according to Equation (15) which is clearly a sum of the *frequencies of occurrence of gray values* in the image since $g(f)$ in this equation is a function of $h(f)$ and $h(f)$ represents a gray-value histogram (See paragraph 1 and Equations (14) and (15) in section B. Background Threshold Determination).

Applicants respectfully submit that Brummer does not disclose feature (ii). Instead, Brummer discloses *removing* partial volume voxels from the mask images as these partial volume voxels are non-brain regions (See paragraphs 2 and 6 in section "C. Morphological Operations for Brain Contour Detection) and *removing* voxels from the images to restore object contours of the original mask (See paragraph 5 in section "C. Morphological Operations for Brain Contour Detection" and Fig. 12(g) which clearly illustrates a decrease in the number of object voxels after the dilated label image in Fig. 12(f) is masked with the original binary image to restore the object contours of the original mask).

In view of the above, Applicants respectfully submit that both claims 1 and 21 are novel over Brummer.

Non-Obviousness of Claims 1 and 21

Applicant respectfully submits that features (i) and (ii) defined in both claims 1 and 21 are non-obvious in view of the cited documents.

With regard to feature (i), as mentioned above, Brummer does not teach or suggest feature (i). In fact, Brummer teaches away from feature (i) by teaching the step

of *maximizing a different function* to obtain a threshold for separating image objects from the background.

With regard to feature (ii), although Brummer discloses the problems created by partial volume effects and morphological openings, it merely teaches the solution of *removing* voxels which were wrongly included in the mask image due to these problems and does not teach or suggest the solution of *restoring* voxels which were wrongly omitted from the set of object voxels due to these problems. Hence, a person skilled in the art would not be led to feature (ii) after reading Brummer.

In view of the above, Applicants respectfully submit that claims 1 and 21 are novel and non-obvious over the cited documents and are hence allowable.

Rejection of Claims 2 – 5, 7 and 9 Under 35 U.S.C. § 102(b)

As stated above, claim 1 is believed to be allowable in view of the cited documents. Dependent claims 2 – 5, 7 and 9 are also allowable at least due to their dependency from main claim 1.

Rejection of Claims 10 – 20 Under 35 U.S.C. 103(a)

Claims 10 – 20 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Brummer as applied to claim 1 and further in view of Nowinski ("A locus-driven mechanism for rapid and automated atlas assisted analysis of functional images by using the Brain Atlas for Functional Imaging," Wieslaw L. Nowinski, et al., Neurosurg Focus 15(1): Article 3, July 15, 2003, pages 1 – 7 listed in IDS).

As stated above, amended claim 1 is believed to be allowable in view of the cited documents. Dependent claims 10 – 20 are also allowable at least due to their dependency from main claim 1.

Furthermore, claims 15 and 19 define conditions determining the classification of voxels as object voxels whereas claim 18 defines a seeding operation to identify object

voxels. Applicant respectfully disagrees with the Examiner that Brummer teaches the features of these claims. With regard to claims 15 and 19, the "connectivity" section in page 158 and the "Labeling of Connected components" and "Dilation of Label Image" sections in page 159 of Brummer (as quoted by the Examiner) are mere definitions of what these morphological operations are and do not teach or suggest how to classify voxels. With regard to claim 18, section "V Morphological Operations" of Brummer does not even teach or suggest any seeding operation. Therefore, not only are claims 15, 18 and 19 allowable as being dependent on an allowable main claim, the features of claims 15, 18 and 19 further patentably distinguish over the cited documents

Claim 20 defines *inter alia*, "the *left and right halves* of the brain are *treated separately*, and the object voxels used to obtain the location of the I landmark relate to a selected half of the brain, the selected half of the brain having been selected based on a predefined criterion". Applicant respectfully disagrees with the Examiner that Brummer discloses this feature. In the last paragraph of the left column in page 157 (as quoted by the Examiner), Brummer discloses that the brain is known to be located predominantly in the superior portion of the head and the extent of what is the *superior half* of the head can be estimated whereas the remainder of the head mask can be *discarded*. A person skilled in the art would understand that the motivation behind treating the left and right halves of the brain separately and using only the superior half of the head for further processing is very different and hence would not be led to implement the features of claim 20 after reading Brummer. Therefore, not only is claim 20 is believed to be allowable as being dependent on an allowable main claim, the features of claim 20 further patentably distinguish over the cited documents.

CONCLUSION

In light of the present amendments and remarks, Applicant respectfully submits that the present claims are in condition for allowance.

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Attorney Docket No. 8249-85693

The Commissioner is hereby authorized to charge any additional fees which may be required in this application under 37 C.F.R. §§ 1.16-1.17 during its entire pendency, or credit any overpayment, to Deposit Account No. 06-1135.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY



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APPENDIX

1. REPLACEMENT SHEETS 1/5-5/5

REPLACEMENT SHEET
Serial No. 10/550,366

1/5

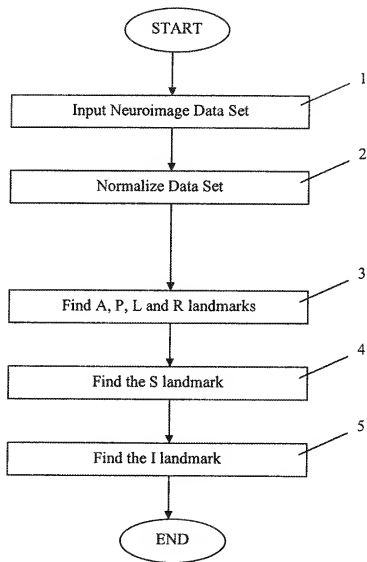


Fig. 1

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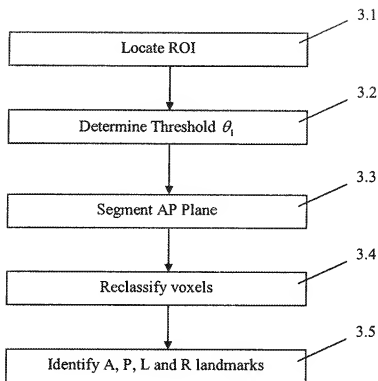


Fig. 2

REPLACEMENT SHEET
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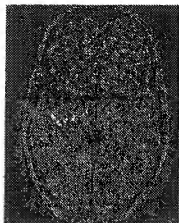


FIG. 3a

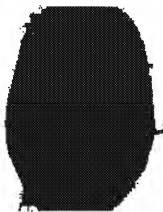


FIG. 3b



FIG. 3c

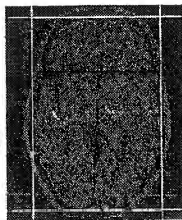


FIG. 3d

REPLACEMENT SHEET

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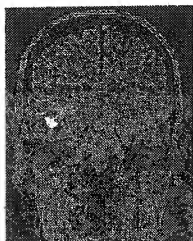


FIG. 4a

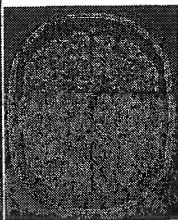


FIG. 4b

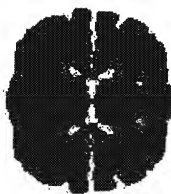


FIG. 4c

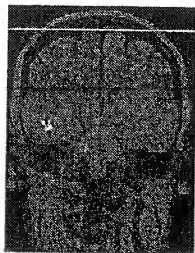


FIG. 4d

REPLACEMENT SHEET
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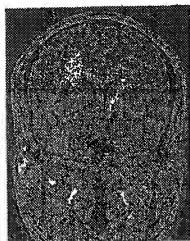


FIG. 5a



FIG. 5b



FIG. 5c

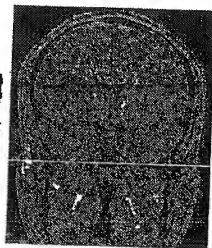


FIG. 5d